

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
PATENT

Applicant : Donovan, Stephen)
)
Serial No.: to be assigned) Examiner:
(Parent App. 09/489,667)) (Parent App. C. Kam, Ph.D.)
)
Filed : herewith) Group Art Unit:
(Parent App. January 19, 2000) (Parent App. 1653)
)
For : CLOSTRIDIAL TOXIN)
DERIVATIVES AND METHODS)
FOR TREATING PAIN)

Box New App Fee
Assistant Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Dear Sir:

Please amend the subject application as follows:

In the Specification:

Please insert the following paragraph before the paragraph beginning at page 1, line 13:

This application is a divisional application of U.S. Serial No. 09/489,667, filed January 19, 2000, the content of which in its entirety is incorporated by reference into the present application.

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In the Claims:

Please cancel claims 1-20, 26-35, and 38-66 without prejudice.

Applicant reserves the right to pursue the subject matter of these claims in a related application in the future at Applicant's discretion.

Please add claims 67-80 as follows:

67. (new) A method for obtaining an agent for alleviating pain, the method comprising:
 - (a) producing a genetic construct having codes for a clostridial neurotoxin component;
 - (b) incorporating the construct into a host organism;
 - (c) expressing the construct to produce the clostridial neurotoxin component; and
 - (d) covalently attaching the clostridial neurotoxin component to substance P.
68. (new) The method of claim 67, further comprising covalently attaching at least one spacer component between the clostridial neurotoxin component and substance P.
69. (new) The method of claim 67, wherein the clostridial neurotoxin component is produced by an organism selected from the group consisting of Clostridial beratti, Clostridial butyricum, Clostridial botulinum, and Clostridial tetani.

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70. (new) The method of claim 67, wherein the clostridial neurotoxin component is a botulinum toxin selected from the group consisting of serotype A, serotype B, serotype C1, serotype D, serotype E, serotype F, and serotype G.
71. (new) The method of claim 67, wherein the clostridial neurotoxin component is botulinum toxin serotype A.
72. (new) The method of claim 67, wherein the clostridial neurotoxin component comprises an H_N and an L chain.
73. (new) The method of claim 72, wherein the H_N is produced by an organism selected from the group consisting of Clostridial beratti, Clostridial butyricum, Clostridial botulinum, and Clostridial tetani.
74. (new) The method of claim 72, wherein the L chain is produced by an organism selected from the group consisting of Clostridial beratti, Clostridial butyricum, Clostridial botulinum, and Clostridial tetani.
75. (new) The method of claim 72, wherein the H_N is obtained from a botulinum toxin selected from the group consisting of botulinum toxin serotype A, serotype B, serotype C1, serotype D, serotype E, serotype F, and serotype G.

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76. (new) A method for obtaining an agent for alleviating pain, the method comprising:
- (a) producing a genetic construct having codes for botulinum toxin;
 - (b) incorporating the construct into a host organism;
 - (c) expressing the construct to produce the botulinum toxin; and
 - (d) covalently attaching the botulinum toxin to substance P.
77. (new) A method for obtaining an agent for alleviating pain, the method comprising:
- (a) producing a genetic construct having codes for a botulinum toxin serotype A;
 - (b) incorporating the construct into a host organism;
 - (c) expressing the construct to produce the botulinum toxin serotype A; and
 - (d) covalently attaching the botulinum toxin serotype A to substance P.

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78. (new) A method for obtaining an agent for alleviating pain, the method comprising:
- (a) producing a genetic construct having codes for a botulinum toxin, wherein the portion encoding an Hc of the toxin has been removed;
 - (b) incorporating the construct into a host organism;
 - (c) expressing the construct to produce the botulinum toxin; and
 - (d) covalently attaching the botulinum toxin to substance P.
79. (new) A method for obtaining an agent for treating pain, the method comprising:
- (a) producing a genetic construct having codes for (1) a clostridial neurotoxin component and (2) substance P;
 - (b) incorporating the genetic construct into a host organism; and
 - (c) expressing the genetic construct to obtain a fusion protein comprising the clostridial neurotoxin component covalently coupled to the substance P.
80. (new) The method of claim 79, wherein the genetic construct includes genetic codes that encode for a spacer component between the clostridial neurotoxin component and substance P.

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Support for the Claims:

Support for claim 67 may be found in the specification at page 30, lines 4-22; and in claims 21 and 25.

Support for claim 68 may be found in the specification at page 30, lines 15-16 and 20-22; and in claim 22.

Support for claim 69 may be found in the specification at page 15, lines 19-21.

Support for claim 70 may be found in the specification at page 15, lines 23-24.

Support for claim 71 may be found in the specification at page 15, lines 23-24.

Support for claim 72 may be found in the specification at page 29, lines 18-30.

Support for claim 73 may be found in the specification at page 29, lines 21-27.

Support for claim 74 may be found in the specification at page 22, line 30 to page 23, line 13.

Support for claim 75 may be found in the specification at page 22, line 30 to page 23, line 13.

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Support for claim 76 may be found in the specification at page 17, lines 8-10; and in claims 21 and 66.

Support for claim 77 may be found in the specification at page 17, lines 8-10; and in claims 21 and 66.

Support for claim 78 may be found in the specification at page 17, lines 10-15.

Support for claim 79 may be found in the specification at page 30, lines 4-22; and in claims 23 and 25.

Support for claim 80 may be found in the specification at page 30, lines 15-16 and 20-22; and in claim 22.

Remarks

The amendment to the specification simply addresses the priority claim of the instant application. The parent application, U.S. Serial No. 09/489,667, is relied on for an earlier effective filing date under 35 U.S.C. § 120. No new matter has been added.

Applicant has canceled claims 1-20, 26-35, and 38-66, as set forth above. Applicant has added claims 67-80, as set forth above. Accordingly, claims 21-25, 36, 37, and 67-80 are currently pending.

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The currently pending claims correspond to the claims of Group II as set forth in the Restriction Requirement dated December 20, 2000 in the related parent application, U.S. Serial No. 09/489,667.

Claims 67-80 are directed to methods of making the agents claimed in claims 69-80 that were filed in the parent application, U.S. Serial No. 04/489,667, in the Amendment dated April 20, 2001. The Examiner of the parent application has indicated that claims 69-80 of the parent application are allowed in the Office Action dated July 11, 2001.

Applicant respectfully submits that the currently pending claims are in condition for allowance.


1. *What is the purpose of the study?*
 2. *What are the research questions or hypotheses?*
 3. *What is the study design?*
 4. *What is the sample size and how was it selected?*
 5. *What are the variables being studied?*
 6. *What are the data collection methods?*
 7. *What are the results of the study?*
 8. *What are the conclusions and implications of the study?*
 9. *What are the limitations of the study?*
 10. *What are the strengths of the study?*
 11. *What are the future research directions?*
 12. *What are the ethical considerations?*
 13. *What are the funding sources?*
 14. *What are the conflicts of interest?*
 15. *What are the acknowledgments?*
 16. *What are the references?*
 17. *What are the appendices?*
 18. *What are the footnotes?*
 19. *What are the tables and figures?*
 20. *What are the conclusions?*

Respectfully submitted,

AUGUST 23, 2001

Handwritten signature: *Handwritten signature*

CERTIFICATE OF MAILING


Jean F. Heuler, August 23, 2001

Jean F. Heuler, August 23, 2001

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

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In the Claims:

Claims 1-20, 26-35, and 38-66 have been canceled.

Claims 67-80 have been added as follows:

67. (new) A method for obtaining an agent for alleviating pain, the method comprising:
- (a) producing a genetic construct having codes for a clostridial neurotoxin component;
 - (b) incorporating the construct into a host organism;
 - (c) expressing the construct to produce the clostridial neurotoxin component; and
 - (d) covalently attaching the clostridial neurotoxin component to substance P.

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68. (new) The method of claim 67, further comprising covalently attaching at least one spacer component between the clostridial neurotoxin component and substance P.
69. (new) The method of claim 67, wherein the clostridial neurotoxin component is produced by an organism selected from the group consisting of Clostridial beratti, Clostridial butyricum, Clostridial botulinum, and Clostridial tetani.
70. (new) The method of claim 67, wherein the clostridial neurotoxin component is a botulinum toxin selected from the group consisting of serotype A, serotype B, serotype C1, serotype D, serotype E, serotype F, and serotype G.
71. (new) The method of claim 67, wherein the clostridial neurotoxin component is botulinum toxin serotype A.
72. (new) The method of claim 67, wherein the clostridial neurotoxin component comprises an H_N and an L chain.
73. (new) The method of claim 72, wherein the H_N is produced by an organism selected from the group consisting of Clostridial beratti, Clostridial butyricum, Clostridial botulinum, and Clostridial tetani.
74. (new) The method of claim 72, wherein the L chain is produced by an organism selected from the group consisting

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of Clostridial beratti, Clostridial butyricum, Clostridial botulinum, and Clostridial tetani.

75. (new) The method of claim 72, wherein the H_N is obtained from a botulinum toxin selected from the group consisting of botulinum toxin serotype A, serotype B, serotype C1, serotype D, serotype E, serotype F, and serotype G.
76. (new) A method for obtaining an agent for alleviating pain, the method comprising:
- (a) producing a genetic construct having codes for botulinum toxin;
 - (b) incorporating the construct into a host organism;
 - (c) expressing the construct to produce the botulinum toxin; and
 - (d) covalently attaching the botulinum toxin to substance P.
77. (new) A method for obtaining an agent for alleviating pain, the method comprising:
- (a) producing a genetic construct having codes for a botulinum toxin serotype A;
 - (b) incorporating the construct into a host organism;
 - (c) expressing the construct to produce the botulinum toxin serotype A; and
 - (d) covalently attaching the botulinum toxin serotype A to substance P.

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78. (new) A method for obtaining an agent for alleviating pain, the method comprising:
- (a) producing a genetic construct having codes for a botulinum toxin, wherein the portion encoding an Hc of the toxin has been removed;
 - (b) incorporating the construct into a host organism;
 - (c) expressing the construct to produce the botulinum toxin; and
 - (d) covalently attaching the botulinum toxin to substance P.
79. (new) A method for obtaining an agent for treating pain, the method comprising:
- (a) producing a genetic construct having codes for (1) a clostridial neurotoxin component and (2) substance P;
 - (b) incorporating the genetic construct into a host organism; and
 - (c) expressing the genetic construct to obtain a fusion protein comprising the clostridial neurotoxin component covalently coupled to the substance P.
80. (new) The method of claim 79, wherein the genetic construct includes genetic codes that encode for a spacer component between the clostridial neurotoxin component and substance P.